REMARKS

I. Status of the Claims

Claims 1-2 are currently pending. Claims 1-2 have been amended. Support of the amendments is found throughout the specification at, for example, page 21, lines 16-19; and page 23, line 17 to page 24, line 4. No new matter is added by way of these amendments.

II. Rejections under 35 U.S.C. § 103

A. Assateerawatt in View of Donnelly

The Examiner has rejected claim 1 under 35 U.S.C. § 103(a) as being unpatentable over Assateerawatt et al. (Asian Pacific Journal of Allergy and Immunology, 11:85-91, 1993 (IDS)) in view of Donnelly et al. (Journal of Immunology Methods, 176:145-152, 1994 (IDS)). According to the Examiner, Assateerawatt teaches inoculation of infants with a recombinant hepatitis B vaccine, and Donnelly teaches immunization with naked DNA (e.g., DNA encoding hepatitis B virus surface antigen (HBsAg)), inducing both antibody and cell-mediated immune responses. Based on these teachings, the Examiner contends that it would have been obvious for one of ordinary skill in the art to apply a DNA encoding HBsAg in neonates at birth or 1 month with a reasonable expectation of success.

Applicants traverse the rejection and respectfully submit that the Examiner has failed to establish a prima facie case of obviousness. As conceded by the Examiner, Assateerawatt does not teach or suggest immunization with a naked nucleic acid. Donnelly discloses various DNA immunizations across animal models having various target antigens, with an emphasis on viral target antigens. However, Donnelly is silent with respect to immunization of an infant human. Further, Donnelly states that "[t]he therapeutic uses of DNA vaccines are beginning to be explored," and "[t]he extent to which this method [of immunization with DNA] can be applied to proteins not of vertebrate origin, e.g., antigens from bacteria and protozoan parasites, remains to be determined." Donnelly, p. 150. In view of the lack of teaching of immunization of an infant human, the limited knowledge regarding the therapeutic uses of DNA vaccines, and the limited application of immunization with DNA, one skilled in the art would not have been motivated to combine Assateerawatt with Donnelly with a reasonable expectation of success to immunize an infant human with a naked nucleic acid.

As Assateerawatt and Donnelly, considered separately or in combination, do not teach or suggest immunization of an infant human with a naked nucleic acid, Applicants respectfully request withdrawal of the anticipation rejection of claim 1 over Assateerawatt in view of Donnelly.

B. Assateerawatt in View of Donnelly and Further in View of Chisari

The Examiner has also rejected claims 1-2 under 35 U.S.C. § 103(a) as being unpatentable over Assateerawatt in view of Donnelly and further in view of Chisari et al. (Springer Semin Immunopathol, 17:261-282, 1995). According to the Examiner, Chisari suggests that neonates born to HBeAg-positive mothers are effectively protected against HBV infection when immunized with the HBsAg vaccine and that HBV envelope-specific T and B cells are still present and functional. Since Assateerawatt noted that infant serum samples of the vaccinated neonates tested for HBsAg antibody titer declined gradually by use of the protein vaccine and Donnelly teaches that DNA vaccines induce both humoral and cellular immune response, the Examiner contends that one of ordinary skill in the art would have been motivated to apply the HBeAg to the HBsAg DNA vaccine of Assateerawatt and Donnelly.

Applicants traverse the rejection and respectfully submit that the Examiner has failed to establish a prima facie case of obviousness. First, the statement by Chisari regarding infants born to HBeAg-positive mothers cites Beasley, but Chisari misinterpreted Beasley, which was cited to support the proposition that "neonates born to HBeAg-positive mothers are effectively protected against HBV infection when immunized with the HBsAg vaccine." Chisari, p. 272. Contrary to Chisari's interpretation, Beasley et al. (Hepatology 3:135-141, 1983; abstract attached as Exhibit A) reports an efficacy trial of hepatitis B immune globulin ("HBIG") for prevention of the mother-to-infant transmitted HBsAg carrier state by monitoring the carrier rate of infants given HBIG, which is neither a HBsAg vaccine nor a naked nucleic acid. Beasley, abstract. Second, although Chisari does state that "it is well known that newborn infants respond quite well to immunization with HBsAg," Chisari does not teach or suggest immunization of neonates with a naked nucleic acid. Further, as set forth above, Assateerawatt and Donnelly, considered separately or in combination, do not teach or suggest immunization of an infant human with a naked nucleic acid. Therefore, Assateerawatt, Donnelly and Chisari, considered separately or in combination, do not teach or suggest the subject matter of claims 1-2.

Accordingly, Applicants respectfully request withdrawal of the anticipation rejection of claims 1-2 over Assateerawatt in view of Donnelly and further in view of Chisari.

III. Conclusion

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Withdrawal of all rejections is requested.

Respectfully submitted,

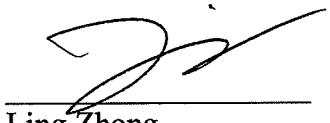

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EXHIBIT A

1: Hepatology. 1983 Mar-Apr;3(2):135-41.

Links

Efficacy of hepatitis B immune globulin for prevention of perinatal transmission of the hepatitis B virus carrier state: final report of a randomized double-blind, placebo-controlled trial.

Beasley RP, **Hwang LY**, **Stevens CE**, **Lin CC**, **Hsieh FJ**, **Wang KY**, **Sun TS**, **Szmuness W**.

A randomized double-blind, placebo-controlled efficacy trial of hepatitis B immune globulin (HBIG) for prevention of the mother-to-infant transmitted HBsAg carrier state was conducted in Taiwan where the carrier rate in the general population is 15 to 20%. HBIG was given immediately after birth to infants of e antigen positive HBsAg carrier mothers, and all infants were followed for at least 15 months. Among 61 placebo recipients, the carrier rate was 92%; compared with 26% among 57 infants who received 0.5 ml HBIG at birth, 3 months, and 6 months, and 54% among 67 infants who received a single 1.0 ml dose of HBIG at birth only. Efficacy was 71 and 42%, respectively, for the two treatment schedules. The most common response of HBIG-treated infants was passive-active immunization which was 27% in the single-dose group and 61% in the three-dose group. Some of the infants who became carriers were probably infected as HBIG protection waned, and we expect that higher efficacy can be achieved by hepatitis B vaccine in conjunction with HBIG.

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